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EXAMINER

GABEL, GAILENE

ART UNIT PAPER NUMBER

1641

DATE MAILED: 03/13/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/912,266

Applicant(s)

FLEMING ET AL.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 December 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 9-24,27 and 28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-24,27 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6.                      6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group II, claims 9-24, 27, and 28, without traverse, filed 12/19/02 in Paper No. 8 is acknowledged and has been entered. Claims 1-8, 25, 26, and 29-33 have been cancelled. Currently, claims 9-24, 27, and 28 are pending and are under examination.

### ***Trademark Usage***

2. The use of the trademark "Oregon Green<sup>TM</sup>" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9-24, 27, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite in reciting, "thereby detecting viable cells in a sample" because as recited, it is unclear what determines the viability of the cells. Perhaps Applicant intends, "thereby, indicating viability of cells in the sample". Further, "a sample" in claim 9, last line, has improper antecedent basis problem.

In claim 9, line 3, the recitation of "a viable cell" is not clear as to whether the cell containing the dye is performing the enzymatic activity or a viable cell that does not contain the dye. Please clarify.

Claim 12 lacks antecedent support in reciting, "said total cell count."

Claim 12 is indefinite in reciting, "UV". Acronyms or abbreviations must be fully defined and recited at least one time in a set of claims.

Claim 15 is indefinite in reciting, "Oregon Green<sup>TM</sup>". Trademark's compounds in claims need to be identified by their generic terminology.

In claim 16, "fluorometer" should be "fluorometer".

In claim 17, the recitation of "providing a sample" has improper antecedent basis problem.

Claim 17 is vague and indefinite in reciting, "thereby detecting the number of viable cells in said sample" because as recited, it is unclear what determines the viability of the cells. Perhaps Applicant intends, "thereby, indicating the viability of a number of cells in the sample".

In claim 17, it is unclear what structural and functional cooperative relationship exists between the "number of viable cells" and the recitation of "a value". Does

Applicant intend “a value” to encompass “number of viable cells”, “number of viable cells and nonviable cells”, or “number of nonviable cells”.

Claim 17 lacks clear antecedent support in reciting, “the detected viable cell value.”

Claim 17, lines 4-6 is confusing because it is unclear how correlating the number of detected viable cells with a standard value provides a quantitation of the number of viable cells in the sample, when the mere detection of the enzymatically altered dye in viable cells, i.e. “detecting the number of viable cells”, would have readily and already provided the quantitation of the viable cells in the sample, which is what is required by the preamble. Accordingly, it is unclear what is intended by the correlation step in the claim.

In claim 17, line 3, “ezymatically” should be --enzymatically--.

Claim 20 lacks antecedent support in reciting, “said total cell count.”

Regarding claim 27, the phrase “or other methods of counting” renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by “or the like”), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

In claim 24, “flurorometer” should be “fluorometer”.

Claim 27 is confusing in reciting, “instructions ... that correlate to hemocytometer counts, plate counts, or other ...” because it is unclear what Applicant intends to encompass by such a recitation. Specifically, how do instructions correlate to “hemocytometer counts, plate counts, or other ...”.

Claim 28 is indefinite in reciting, "following penetration of viable cells" because it appears that the viable cells penetrate a dye. Perhaps, Applicant intends, "following penetration into viable cells".

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or  
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 9-12, 14, 15, 17-20, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Breeuwer et al. (Applied and Environmental Microbiology 60(5): 1467-1472 (May 1994).

Breeuwer et al. teach a method for detecting cell viability using flow cytometry. Breeuwer et al. specifically teach contacting (vital staining) a sample containing yeast cells or bacterial cells with (carboxy)fluorescein diacetate which is a dye that diffuses into (translocates) or is transported into the cells. In the cell, the fluorescein diacetate dye is detectably altered by enzyme esterase activity (hydrolysis by nonspecific esterases) that takes place inside the viable cells in the sample. Fluorescein diacetate

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is retained by viable cells with intact membrane and lost by cells with damaged membrane. In practice, Breeuwer et al. determined viability of *Saccharomyces cerevisiae* by loading the yeast cells with fluorescein diacetate, followed by incubation at 40C in the presence of glucose. Thereafter, fluorescence intensity of the cells was analyzed and quantitated by flow cytometry (see Abstract). According to Breeuwer et al., dye (methylene blue) exclusion test and plate count methods are other tests for detecting or assessing viability (see page 1467, column 1).

4. Claims 9, 11, 12, 14, 16, 17, 19, 20, 22, 24, 27, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Sarkadi et al. (US 6,277,655).

Sarkadi et al. disclose a method and kit for detecting viability of cells versus non-viability of cells. Sarkadi et al. disclose contacting the animal or yeast (fungal) cells with non-fluorescent form of calcein AM dye that diffuses into cell (membrane permeant dye). Inside viable cells, calcein AM is detectably altered into a fluorescent form, i.e. free calcein, by intracellular esterase enzymes (see column 10, lines 53-67 and column 6, lines 4-43). The fluorescent calcein accumulated in the cells is determined by fluorescent measurement using a fluorometer (see column 9, lines 12-24). The kit for use in the method includes calcein AM dye and instructions for carrying out the method for detecting viability of the cells.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 13 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breeuwer et al. (Applied and Environmental Microbiology 60(5): 1467-1472 (May 1994) or Sarkadi et al. (US 6,277,655) in view of Katz (US 3,586,859).

Breeuwer et al. or Sarkadi et al. have been discussed supra. Breeuwer et al. or Sarkadi et al. differ from the instant invention in failing to disclose determining total cell count using UV absorption measurement.

Katz discloses detecting both viable cells and nonviable cells in a sample. Specifically, Katz discloses contacting the cells with a fluorescent dye, obtaining a count of the cells that fluoresce under a microscope (dead cells), killing all the cells using heat, then determining the total count of all the cells by ultraviolet absorption measurement (see Summary in column 1).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Katz in determining specifically the total count of cells including both viable cells and non-viable cells using UV absorption measurements, into the method of determining the amount of viable cells in a sample as taught by Breeuwer or Sarkadi because Katz specifically taught that a total amount of both viable and non-viable cells can be obtained by first measuring non-viable cells, the difference of which is reflective of the number of viable cells, then killing the viable cells



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using heat in order to obtain a total count of all the cells in the sample using UV absorption measurements.

6. No claims are allowed.

**Remarks**

7. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Breeuwer et al. (Applied and Environmental Microbiology, 61(4): 1614-1619 (April 1995)) teach characterization of uptake and hydrolysis of fluorescein diacetate and carboxyfluorescein diacetate by intracellular esterases in *S. cerevisiae*, which results in accumulation of fluorescent product (see Abstract).

Steward et al. (Plant Cell Reports 17: 171-176 (1999)) teach assessing plant cell viability using intracellular esterase activity upon fluorescein diacetate as substrate (see Abstract).

Harman et al. (US 5,939,282) disclose a method of assessing viability of cells in microbial cultures using fluorescein diacetate, carboxyfluorescein diacetate, or calcein AM as membrane permeable stain for live viable cells (see Abstract and column 3).

Redelman et al. (WO 92/02632) disclose a method for detecting, identifying, and enumerating viable cells in bovine milk samples using esterified esterase-dependent dyes including derivatives of fluorescein diacetate dyes (see Summary and pages 12-13).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday, 6:30-1630, and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel  
Art Unit 1641  
March 8, 2003 *gfb*

*Christopher L. Chin*  
CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1800/1641  
3/9/03